REMARKS

A. Status of the Claims

Claims 8, 20-25 and 44-56 are pending, of which claims 25, 44-45, 48-50, 52-55 are withdrawn. Claim 56 has been amended. Thus, claims 8, 20-25, 46-47, 51 and 56 are under examination.

B. Section 112, First paragraph (Enablement) Concerns

All of the claims under examination have been rejected as lacking enablement. In making this rejection, the Examiner's underlying premise is that "the claimed invention [concerns] substituting or adding one or more of the recited non-natural amino acid residue(s) to a peptide that is not already a CTL epitope in order to obtain a peptide antigen." Office Action, page 3.

The underlying premise of the rejection is incorrect: the present invention is directed to a method of improving *known* antigens by incorporating therein one or more of the non-natural amino acids specified in claim 8. This is evident from the first sentence of the summary: "In one aspect, the invention provides a method ***for preparing a peptide antigen with modulated immunogenicity comprising substituting at least a first amino acid located in a CTL epitope with a first substitute amino acid*** having an extended or shortened side chain as compared to the first amino acid." (emphasis ours).

Curiously, the Examiner then contradicts this position by stating that the specification ***does*** teach how to carry out the invention and improve upon ***known*** antigens:

> Thus, the specification teaches selecting the amino acid residue to be substituted by the position it occupies in a peptide (that is already known to be a CTL epitope), the direction of its side chain orientation relative to the peptide binding groove of MHC class I, and the nature of the amino acid residue at the position to be substituted, in order to determine if the amino acid residue can potentially be

> substituted with a non-natural amino acid residue, and what the nature of that substitution might be, in order to influence such properties as cytokine induction, cross-reactivity, peptide-induced CTL lytic activity and affinity. The specification also teaches actually assessing these indices for the E75 peptide to determine if it is a still a peptide antigen.

Office Action at page 3-4. Accordingly, the Examiner's statement that there is insufficient teaching in the specification is simply incorrect. The MPEP requires that in order to make a *prima facie* rejection, the Examiner must set forth a reasonable explanation as to why the claim(s) are not adequately enabled. MPEP 2164.04 Here, the foregoing excerpt from the Office Action itself demonstrates precisely why the rejection is improper, and evidences why one of skill in the art would be fully enabled to carry out the invention.

Moreover, in that the invention is concerned with modifying known epitopes, we would point out the great detail that is provided for identifying known CTL epitopes in proteins – a practice that is *exceedingly* well known. Indeed, there are numerous techniques and available commercial products for doing so that are set forth in the specification at paragraphs [0047] and [0048] of the published application, 2005/0169934. We would further refer the Examiner to the entire section B entitled "Identifying CTL Epitopes".

The relevance of the Examiner's reliance on Rodkey and the differences between an immunogen and an antigen is not understood and not relevant here as it merely evidences that Rodkey's definitions are not necessarily consistent with those used in the present application, which uses "immunogenicity", "antigenicity" and "antigen" interchangeably. See, for example, Section H of the specification entitled "Modified CTL Epitopes."

Lastly, the Action states (without support) that it is unpredictable which amino acids are to be modified. This again is contrary to the Examiner's above statement that" the specification teaches selecting the amino acid residue to be substituted by the position it occupies in a peptide (that is already known to be a CTL epitope), the direction of its side chain orientation relative to

the peptide binding groove of MHC class I, and the nature of the amino acid residue at the position to be substituted, in order to determine if the amino acid residue can potentially be substituted with a non-natural amino acid residue." Furthermore, we would point out that the specification teaches specific methods for identifying the most preferred positions for such a modification. See, *e.g.*, paragraph [0048] as well as the entire section H, entitled "Modified CTL Epitopes" which goes into great detail on this subject, and even provide exemplary substitutions (see, pages 6-8 of the published application, and particularly Tables 1 and 2.

For at least the foregoing reasons, it is clear that the Action fails to make out a *prima facie* rejection as required by MPEP 2164.04. If there are particular claim amendments that the Examiner believes might address the rejection, Applicants would be pleased to discuss such amendments in an after-final interview. If such is the case, a telephone call to the undersigned is earnestly solicited.

C. Section 112, Second Paragraph Concerns

A slight amendment to claim 56 has been made, which is believed to address the Examiner's concerns.

D. 35 U.S.C. §102(b) Concerns

The action rejects claims 8, 20-22, 45, 46 and 51 as anticipated under 35 U.S.C. §102(b) over the Carter *et al.* ("Carter") abstract.

In response, Applicants note that Carter reference, a reference published on behalf of the present inventive entity, was published March 8, 2001. However, Applicants would note that the present case has a priority of March 8, 2002 by virtue of provisional application serial number 60/362,778. Therefore, the Carter reference is unavailable under 35 U.S.C. §102(b). If the Examiner elects to re-open prosecution and re-assert the Carter reference under 35 U.S.C.

§102(a), Applicants will agree to file an appropriate Katz declaration to remove the reference. Applicants preference, however, would be to handle this at the present time if the Examiner is willing.

E. Rejoinder/Conclusion

The Examiner is requested to now rejoin the withdrawn claims, as foregoing is believed to be a complete response to the Office Communication and is believed to place the case into condition for allowance. The Examiner is invited to contact the undersigned attorney at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

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